REMARKS

Pending Claims

Applicants acknowledge claims 2, 4, 5, 12, 15-16, 25, 27, 34-37, 39, 40, 42 and 45-47 are pending in the application and the withdrawal of the rejection under 35 USC 103 over Atwal. Reconsideration of obviousness type double patenting rejection over US 7371763 and copending application 11/932269 is respectfully requested.

The rejection for obviousness type double patenting is based on claims 1 and 21 of US Patent No. 7,371,763 and claims 22 and 23 of copending application number 11/932269. These claims are attached hereto as Appendix A for reference.

In the last response, Applicants argued that the subject matter claimed herein was excluded from the claims of US Patent No. 7,371,763 and copending application number 11/932269 based on the following proviso that appears in claim 1 of US patent No. 7,371,763 and claim 22 of copending application number 11/932269.

> "where B, B' or B" is $-L(ML^1)_q$, L^1 is not substituted by the substituents $-C(O)R^a$, $-C(NR^a)R^b$, $-C(O)NR^aR^b$ and $-SO_2R^a$ wherein each R^a and R^b are independently hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O,"

This proviso excludes the compounds claimed herein by excluding compounds where L^1 is substituted by $-C(O)NR^aR^b$ where R^a and R^b are independently hydrogen or a carbon based moiety of up to 24 carbon atoms with or without heteroatoms selected from N, S and O.

Applicants agree that the proviso does not exclude moieties for R^a and R^b with over 24 carbon atoms but maintain it is effective in excluding the moieties which are required for the compounds claimed herein, and therefore is effective in excluding the compounds claimed herein.

The compounds claimed herein are ureas of the formula: A - D – B, where D is the urea group, A is of the formula: $-L-(M-L^1)_q$ and B is (optionally substituted) pyridyl, quinolinyl or isoquinolinyl.

The moiety L^1 of A is phenyl or pyridinyl substituted by $-C(O)R_x$, where

R_x is NR^aR^b.

The moieties R^a and R^b are limited to hydrogen and other substituents which all contain carbon. These are repeated below.

1) C_1-C_{10} alkyl, (10-carbon atoms)

2) C_{3-10} cycloalkyl, (10-carbon atoms)

3) C_{2-10} alkenyl, (10-carbon atoms)

4) C_{1-10} alkenoyl, (10-carbon atoms)

5) phenyl, (6-carbon atoms)

6) pyridinyl, (5-carbon atoms)

7) piperazinyl, (4-carbon atoms)

8) morpholinyl, (4-carbon atoms)

9) piperidinyl, (5-carbon atoms)

10) pyrrolidinyl, (4-carbon atoms)

11) tetrahydrofuryl, (4-carbon atoms)

12) substituted C_{1-10} alkyl, (10-carbon atoms plus substituents)

13) substituted C_{3-10} cycloalkyl, (10-carbon atoms plus substituents)

14) substituted phenyl, (6-carbon atoms plus substituents)

15) substituted pyridinyl, (5-carbon atoms plus substituents)

16) substituted piperazinyl, (4-carbon atoms plus substituents)

17) substituted morpholinyl, (4-carbon atoms plus substituents)

18) substituted piperidinyl, (4-carbon atoms plus substituents)

19) substituted pyrrolidinyl, (4-carbon atoms plus substituents)

or

20) substituted tetrahydrofuryl, (4-carbon atoms plus substituents)

The suitable substituents for R_a and R_b do not provide totals of over 24 carbon atoms such that the proviso language clearly excludes the compounds claimed herein.

If the definition of R^a and R^b herein is interpreted to include moieties in excess of 24 carbon atoms where R^a and R^b have multiple substituents, the compounds formed would not provide a basis for an obviousness type double patenting rejection. There is no evidence the disclosure in US 7371763 and copending application 11/932269 provide for compounds wherein R^a and R^b are moieties with over 24 carbon atoms. For example, copending application 11/932269 defines R^a and R^b on page 5, lines 13-22 as follows:

wherein R^a and R^b are each, independently, hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O.

R^a and R^b are preferably C_{1-10} alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl having 0-3 heteroatoms, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{7-24} aralkyl, C_{7-24} alkaryl, substituted C_{1-10} alkyl, substituted C_{1-10} alkoxy, substituted C_{3-10} cycloalkyl having 0-3 heteroatoms selected from N, S and O, substituted C_6 -C_{14} aryl, substituted C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, substituted C_{7-24} alkaryl or substituted C_7-C_{24} aralkyl, where R^a is a substituted group, it is substituted by halogen up to per halo. emphasis added.

This definition does not provide for moieties with over 24 carbon atoms and the substituents for R^a and R^b do not add to the carbon count in that they are limited to halogen.

A similar definition appears at column 3, line 60 through column 4, line 7 of US 7371763.

In view of the significant structural distinctions between the compounds claimed herein and those of US 7371763 and copending application 11/932269 mandated by the proviso language, the pending claims herein are patentably distinct from the subject matter claimed in US 7371763 and copending application 11/932269. In view of these distinctions, Applicants respectfully submit the rejection under the doctrine of obviousness type double patenting should be withdrawn.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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Attorney Docket No.: **BAYER-0015-P03**

Date: **December 1, 2010**

APPENDIX A

Claims 1 and 21 of US Patent No. 7371763

1. A compound of one of the following formulae

A - D - B (I)

A'- D - B' (II) and

A"-D-B" (III)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is selected from the group consisting of substituted t-butylpyridyl groups, unsubstituted t-butylpyridyl groups, substituted (trifluoromethyl) pyridyl groups, unsubstituted (trifluoromethyl) pyridyl groups, substituted isopropylpyridyl groups, unsubstituted isopropylpyridyl groups, substituted (2-methyl-2-butyl) pyridyl groups, unsubstituted (2-methyl-2-butyl pyridyl) groups, substituted (3-methyl-3-pentyl) pyridyl groups, and unsubstituted (3-methyl-3-pentyl) pyridyl groups, substituted (3-ethyl-3-pentyl) pyridyl groups and unsubstituted (3-ethyl-3-pentyl) pyridyl groups,

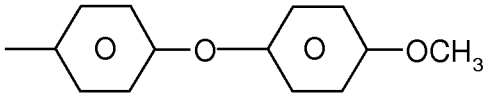
A' is a substituted isoquinolinyl group or unsubstituted isoquinolinyl group or an unsubstituted quinolinyl group,

A" is a substituted quinolinyl group,

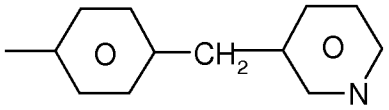
B, B' and B" are each, independently, a substituted or unsubstituted bridged cyclic structure of up to 30 carbon atoms of the formula $-L-(ML^1)_q$ wherein L comprises a cyclic moiety having at least 5 members and is bound directly to D, L^1 comprises a cyclic moiety having at least 5 members, M is a bridging group selected from the group consisting of -O-, -S-, $-N(R^7)-$, $-(CH_2)_m-$, -C(O)-, -CH(OH)-, $-(CH_2)_mO-$, $-(CH_2)_mS-$, $-(CH_2)_m N(R^7)-$, $-O(CH_2)_m$, $-CHX^a-$, $-CX^a_2-$, $-S-(CH_2)_m-$ and $-N(R^7)(CH_2)_m-$, where m=1-3, X^a is halogen, and R^7 is as defined below,

q is an integer of from 1-3, and each cyclic structure of L and L^1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

subject to the provisos that B is not

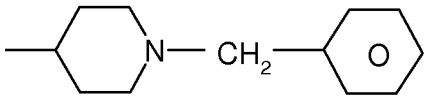


and B' is not



;

or



wherein the substituents for A" and the substituted isoquinolinyl groups of A' are selected from the group consisting of halogen, up to per-halo, and Wn, where n is 0-3 and each W is independently selected from the group consisting of C_{1-10} alkyl, C_{1-10} alkoxy, at least a five membered C_{3-10} cycloalkyl having 0-3 heteroatoms, C_{2-10} alkenyl, C_{1-10} alkenoyl, substituted C_{1-10} alkyl, substituted C_{1-10} alkoxy, at least a five-membered substituted C_{3-10} cycloalkyl having 0-3 heteroatoms selected from N, S and O; -CN, up to per halo substituted C_6-C_{14} aryl, up to per halo substituted C_7-C_{24} alkaryl, up to per halo substituted C_7-C_4 aralkyl, up to per halo substituted C_3-C_{12} heteroaryl having at least 5 members and 1-3 heteratoms selected from O, N and S, up to per halo substituted C_4-C_{24} alkheteroaryl having at least 5 members and 1-3 heteroatoms selected from O, N and S, C_6-C_{14} aryl, C_1-C_{24} alkaryl, C_1-C_{24} aralkyl, C_3-C_{12} heteroaryl having at least 5 cyclic members and 1-3 heteroatoms selected from O, N and S, C_4-C_{24} alkheteroaryl having at least 5 cyclic members and 1-3 heteroatoms selected from O, N and S; $-CO_2R^7$, $-C(O)NR^7R^{7'}$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NR^7C(O)OR^{7'}$, $-NR^7C(O)R^{7'}$, with each R^7 and $R^{7'}$ independently selected from hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{2-10} alkenyl, C_{1-10} alkenoyl, up to per halosubstituted C_{1-10} alkyl, up to per halosubstituted C_{1-10} alkoxy, up to per halosubstituted C_{2-10} alkenyl and up to per halosubstituted C_{1-10} alkenoyl;

wherein the substituents for the substituted t-butyl pyridyl groups substituted trifluoromethyl pyridyl groups, substituted isopropyl pyridyl groups, substituted 2-methyl -2-butyl pyridyl groups and substituted 3-methyl-3-pentyl pyridyl groups of A

are selected from the group consisting of halogen, up to per-halo, and Zn, where n is 0-3 and each Z is independently selected from the group consisting of C_{1-10} alkyl, C_{1-10} alkoxy, C_{2-10} alkenyl, C_{1-10} alkenoyl, -CN, $-CO_2R^7$, $-C(O)NR^7R^{7'}$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NR^7C(O)OR^{7'}$, $-NR^7C(O)R^{7'}$, with each R^7 and $R^{7'}$ independently as defined above for W;

where B and B' are substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and Jn, where n is 0-3 and each J is independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)NR^7R^{7'}$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NR^7C(O)OR^{7'}$, $-NR^7C(O)\ R^{7'}$, with each R^7 and $R^{7'}$ independently as defined above for W, C_{1-10} alkyl, C_{1-10} alkoxy, at least a five-membered C_{3-10} cycloalkyl having 0-3 heteroatoms, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, at least a five-membered C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{7-24} aralkyl, C_{7-24} alkaryl, substituted C_{1-10} alkyl, substituted C_{1-10} alkoxy, at least a five-membered substituted C_{3-10} cycloalkyl having 0-3 heteroatoms selected from N, S and O, substituted C_6 - C_{14} aryl, at least a five-membered substituted C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, substituted C_{7-24} alkaryl and substituted C_7-C_{24} aralkyl,

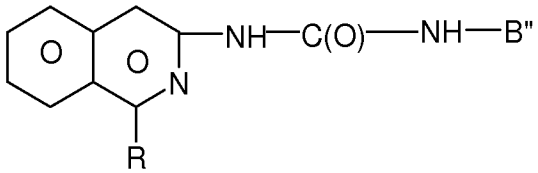
where B" is substituted, the substituents are selected from the group consisting of halogen, -CN, $-C(O)NR^7R^{7'}$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NR^7C(O)OR^{7'}$, $-NR^7C(O)\ R^{7'}$, with each R^7 and $R^{7'}$ independently as defined above for W, C_{1-10} alkyl, at least a five-membered C_{3-10} cycloalkyl having 0-3 heteroatoms, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, at least a five-membered C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{7-24} aralkyl, C_{7-24} alkaryl, substituted C_{1-10} alkyl, substituted C_{1-10} alkoxy, at least a five-membered substituted C_{3-10} cycloalkyl having 0-3 heteroatoms selected from N, S and O, substituted C_6 - C_{14} aryl, at least a five-membered substituted C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, substituted C_{7-24} alkaryl and substituted C_7-C_{24} aralkyl,

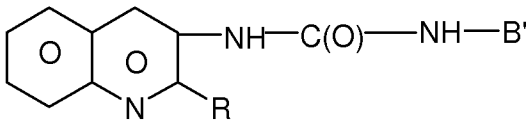
subject to the proviso that where B, B' or B" is $-L(ML^1)_q$, L^1 is not substituted by the substituents $-C(O)R^a$, $-C(NR^a)R^b$, $-C(O)NR^aR^b$ and $-SO_2R^a$ wherein each R^a and R^b are independently hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O,

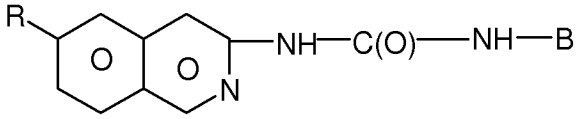
where J is a substituted group, it is substituted by halogen, up to per halo, or by one or more substituents independently selected from the group consisting of -CN,

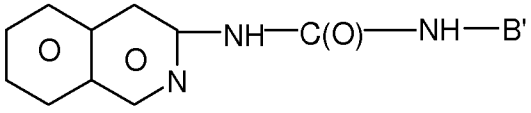
$-CO_2R^7$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NO_2$, $-NR^7C(O)R^{7'}$ and $-NR^7C(O)OR^{7'}$; with each R^7 and $R^{7'}$ independently as defined above for W.

21. A compound of claim 1 of one of the following formulae









wherein B, B' and B" are as defined in claim 1 and R is selected from the group consisting of halogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{2-10} alkenyl, C_{1-10} alkenoyl, -CN, $-CO_2R^7$, $-C(O)NR^7R^{7'}$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NR^7C(O)OR^{7'}$, $-NR^7C(O)R^{7'}$, with each R^7 and $R^{7'}$ are independently selected from hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{2-10} alkenyl, C_{1-10} alkenoyl, up to per halosubstituted C_{1-10} alkyl, up to per halosubstituted C_{1-10} alkoxy, up to per halosubstituted C_{2-10} alkenyl and up to per halosubstituted C_{1-10} alkenoyl.

Claims 21 and 22 of US Application No. 11/932269

21. A method for inhibiting raf kinase in a patient comprising administering an effective amount of a compound of one of the following formulas

A - D - B (I)

A'- D - B' (II) and

A"-D-B" (III)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted t-butylpyridyl group, unsubstituted t-butylpyridyl group, substituted (trifluoromethyl) pyridyl group, unsubstituted (trifluoromethyl) pyridyl group, substituted isopropylpyridyl group, unsubstituted isopropylpyridyl group, substituted (2-methyl-2-butyl) pyridyl group, unsubstituted (2-methyl-2-butyl pyridyl) group, substituted (3-methyl-3-pentyl) pyridyl group, and unsubstituted (3-methyl-3-pentyl) pyridyl group, substituted (3-ethyl-3-pentyl) pyridyl group or unsubstituted (3-ethyl-3-pentyl) pyridyl group,

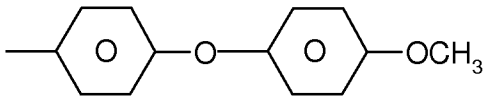
A' is a substituted isoquinolinyl group or unsubstituted isoquinolinyl group or an unsubstituted quinolinyl group,

A" is a substituted quinolinyl group,

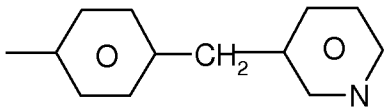
B, B' and B" are each, independently, a substituted or unsubstituted bridged cyclic structure of up to 30 carbon atoms of the formula -L-$(ML^1)_q$ wherein L comprises a cyclic moiety having at least 5 members and is bound directly to D, L^1 comprises a cyclic moiety having at least 5 members, M is a bridging group which is -O-, -S-, -N(R^7)-, -$(CH_2)_m$-, -C(O)-, -CH(OH)-, -$(CH_2)_m$O-, -$(CH_2)_m$S-, -$(CH_2)_m$N(R^7)-, -O$(CH_2)_m$, -CHX^a-, -C$X^a{}_2$-, -S-$(CH_2)_m$- or -N(R^7)$(CH_2)_m$-, where m=1-3, X^a is halogen, and R^7 is as defined below,

q is an integer of from 1-3, and each cyclic structure of L and L^1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur,

subject to the provisos that B is not



and B' is not



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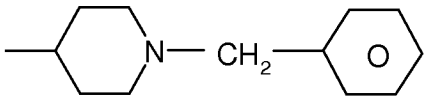
or



wherein the substituents for the quinolinyl groups of A" and the substituted isoquinolinyl groups of A' are selected from the group consisting of halogen, up to per-halo, and Wn, where n is 0-3 and each W is C_{1-10} alkyl, C_{1-10} alkoxy, at least a five membered C_{3-10} cycloalkyl having 0-3 heteroatoms, C_{2-10} alkenyl, C_{1-10} alkenoyl, at least a five-membered methyl substituted C_{3-10} cycloalkyl having 0-3 heteroatoms selected from N, S and O; -CN, up to per halo substituted C_6-C_{14} aryl, up to per halo substituted C_7-C_{24} alkaryl, up to per halo substituted C_7-C_4 aralkyl, up to per halo substituted C_3-C_{12} heteroaryl having at least 5 members and 1-3 heteratoms selected from O, N and S, up to per halo substituted C_4-C_{24} alkheteroaryl having at least 5 members and 1-3 heteroatoms selected from O, N and S, C_6-C_{14} aryl, C_1-C_{24} alkaryl, C_1-C_{24} aralkyl, C_3-C_{12} heteroaryl having at least 5 cyclic members and 1-3 heteroatoms selected from O, N and S, C_4-C_{24} alkheteroaryl having at least 5 cyclic members and 1-3 heteroatoms selected from O, N and S; $-CO_2R^7$, $-C(O)NR^7R^{7'}$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NR^7C(O)OR^{7'}$, or $-NR^7C(O)R^{7'}$, where each R^7 and $R^{7'}$ independently is hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{2-10} alkenyl, C_{1-10} alkenoyl, up to per halosubstituted C_{1-10} alkyl, up to per halosubstituted C_{1-10} alkoxy, up to per halosubstituted C_{2-10} alkenyl or up to per halosubstituted C_{1-10} alkenoyl;

wherein the substituents for the substituted t-butyl pyridyl groups, substituted trifluoromethyl pyridyl groups, substituted isopropyl pyridyl groups, substituted 2-methyl -2-butyl pyridyl groups and substituted 3-methyl-3-pentyl pyridyl groups of A are selected from the group consisting of halogen, up to per-halo, and Zn, where n is 0-3 and each Z is independently C_{1-10} alkyl, C_{1-10} alkoxy, C_{2-10} alkenyl, C_{1-10} alkenoyl, -CN, $-CO_2R^7$, $-C(O)NR^7R^{7'}$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NR^7C(O)OR^{7'}$, or $-NR^7C(O)R^{7'}$, with each R^7 and $R^{7'}$ independently as defined above for W;

where B and B' are substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and Jn, where n is 0-3 and each J is independently -CN, $-CO_2R^7$, $-C(O)NR^7R^{7'}$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NR^7C(O)OR^{7'}$, or $-NR^7C(O)\ R^{7'}$, with each R^7 and $R^{7'}$ independently as defined above for W, C_{1-10} alkyl, C_{1-10} alkoxy, at least a five-membered C_{3-10} cycloalkyl having 0-3 heteroatoms, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, at least a five-membered C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{7-24} aralkyl, C_{7-24} alkaryl, substituted C_{1-10} alkyl, substituted C_{1-10} alkoxy, at least a five-membered substituted C_{3-10} cycloalkyl having 0-3 heteroatoms selected from N, S and O, substituted C_6 - C_{14} aryl, at least a five-membered substituted C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, substituted C_{7-24} alkaryl or substituted C_7-C_{24} aralkyl,

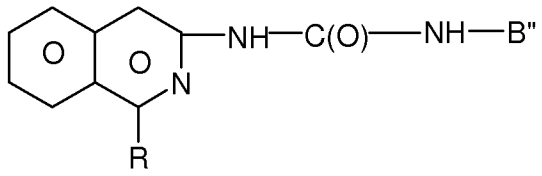
where B" is substituted, the substituents are halogen, -CN, $-C(O)NR^7R^{7'}$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NR^7C(O)OR^{7'}$, $-NR^7C(O)\ R^{7'}$, with each R^7 and $R^{7'}$ independently as defined above for W, C_{1-10} alkyl, at least a five-membered C_{3-10} cycloalkyl having 0-3 heteroatoms, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, at least a five-membered C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{7-24} aralkyl or C_{7-24} alkaryl,

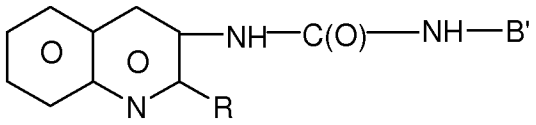
subject to the proviso that where B, B' or B" is $-L(ML^1)_q$, L^1 is not substituted by the substituents $-C(O)R^a$, $-C(NR^a)R^b$, $-C(O)NR^aR^b$ or $-SO_2R^a$ wherein each R^a and R^b are independently hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O,

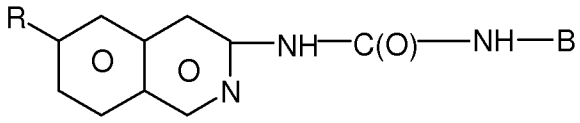
where J is a substituted group, it is substituted by halogen, up to per halo, or by one or more substituents which independently is -CN, $-CO_2R^7$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NO_2$, $-NR^7C(O)R^{7'}$ or $-NR^7C(O)OR^{7'}$; with each R^7 and $R^{7'}$ independently as defined above for W,

to a patient with carcinoma of the lungs, pancreas, thyroid, bladder or colon, myeloid leukemia or villous colon adenoma.

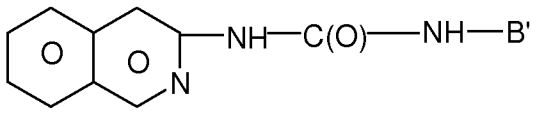
22. A method as in claim 21 for inhibiting raf kinase in a patient, comprising administering an effective amount of a compound of one of the following formulas A-D-B, A'-D-B', A"-D-B",







or



or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)NH-

R is halogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{2-10} alkenyl, C_{1-10} alkenoyl, -CN, $-CO_2R^7$, $-C(O)NR^7R^{7'}$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$; or $-NR^7C(O)OR^{7'}$, $-NR^7C(O)R^{7'}$,

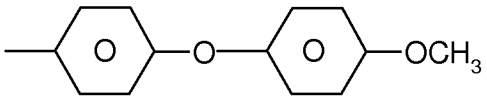
A is a substituted t-butylpyridyl group, unsubstituted t-butylpyridyl group, substituted (trifluoromethyl) pyridyl group, unsubstituted (trifluoromethyl) pyridyl group, substituted isopropylpyridyl group, unsubstituted isopropylpyridyl group, substituted (2-methyl-2-butyl) pyridyl group, unsubstituted (2-methyl-2-butyl) pyridyl group, substituted (3-methyl-3-pentyl) pyridyl group, unsubstituted (3-methyl-3-pentyl) pyridyl group, substituted (3-ethyl-3-pentyl) pyridyl group, or unsubstituted (3-ethyl-3-pentyl) pyridyl group,

A' is a substituted isoquinolinyl group or unsubstituted isoquinolinyl group or an unsubstituted quinolinyl group,

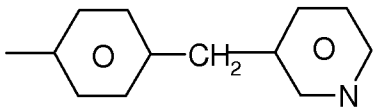
A" is a substituted quinolinyl group,

B, B' and B" are each independently of the formula $-L-(ML^1)_q$, wherein L is phenyl or substituted phenyl and L^1 is phenyl, substituted phenyl, pyridinyl or substituted pyridinyl, q is an integer of from 1-2 and M is -O-, -S-, $-N(R^7)-$, $-(CH_2)_m-$, -C(O)-, -CH(OH)-, $-(CH_2)_mO-$, $-(CH_2)_mS-$, $-(CH_2)_m N(R^7)-$, $-O(CH_2)_m$, $-CHX^a-$, $-CX^a_2-$, -S-(CH_2)- or $-N(R^7)(CH_2)_m-$, where m=1-3, X^a is halogen, and R^7 is as defined below;

subject to the provisos that B is not



and B' is not



;

wherein the substituents for the substituted t-butyl pyridyl groups, substituted trifluoromethyl pyridyl groups, substituted isopropyl pyridyl groups, substituted 2-methylbutyl pyridyl groups and 3-methylpentyl pyridyl groups~~,~~ of A are selected from the group consisting of halogen, up to per-halo, and Zn, where n is 0-3 and each Z is C_{1-10} alkyl, C_{1-10} alkoxy, C_{2-10} alkenyl, C_{1-10} alkenoyl, -CN, $-CO_2R^7$, $-C(O)NR^7R^{7'}$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NR^7C(O)OR^{7'}$or, $-NR^7C(O)R^{7'}$, where each R^7 and $R^{7'}$ independently is hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{2-10} alkenyl, C_{1-10} alkenoyl, up to per halosubstituted C_{1-10} alkyl, up to per halosubstituted C_{1-10} alkoxy, up to per halosubstituted C_{2-10} alkenyl or up to per halosubstituted C_{1-10} alkenoyl;

wherein the substituents for the quinolinyl groups of A" and the substituted isoquinolinyl groups of A' are selected from the group consisting of halogen, up to per-halo, and Wn, where n is 0-3 and each W is independently C_{1-10} alkyl, C_{1-10} alkoxy, C_{2-10} alkenyl, C_{1-10} alkenoyl, -CN, $-CO_2R^7$, $-C(O)NR^7R^{7'}$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NR^7C(O)OR^{7'}$or ~~,~~ $-NR^7C(O)R^{7'}$, where each R^7 and $R^{7'}$ is independently hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{2-10} alkenyl, C_{1-10} alkenoyl, up to per halosubstituted C_{1-10} alkyl, up to per halosubstituted C_{1-10} alkoxy, up to per halosubstituted C_{2-10} alkenyl or up to per halosubstituted C_{1-10} alkenoyl;

wherein B and B' are substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and Jn, where n is 0-3 and each J is independently -CN, $-CO_2R^7$, $-C(O)NR^7R^{7'}$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NR^7C(O)OR^{7'}$~~,~~ or $-NR^7C(O)R^{7'}$, with each R^7 and $R^{7'}$ independently as defined above for W, C_{1-10} alkyl, C_{1-10} alkoxy, C_{2-10} alkenyl, C_{1-10} alkenoyl, substituted C_{1-10} alkyl, ~~and~~ or substituted C_{1-10} alkoxy,

subject to the proviso that where B, B' or B" is $-L(ML^1)_q$, L^1 is not substituted by the substituents $-C(O)R^a$, $-C(NR^a)R^b$, $-C(O)NR^aR^b$ and $-SO_2R^a$ wherein R^a and R^b

are each independently, hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O,

where J is a substituted group, it is substituted by halogen, up to per halo, or by one or more substituents which independently is -CN, $-CO_2R^7$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NO_2$, $-NR^7C(O)R^{7'}$ or $-NR^7C(O)OR^{7'}$; with each R^7 and $R^{7'}$ independently as defined above for W to a patient with carcinoma of the lungs, pancreas, thyroid, bladder or colon, myeloid leukemia or villous colon adenoma,

wherein B" is substituted, the substituents are halogen, -CN, $-C(O)NR^7R^{7'}$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^{7'}$, $-NR^7C(O)OR^{7'}$, $-NR^7C(O)R^{7'}$, with each R^7 and $R^{7'}$ independently as defined above for W, C_{1-10} alkyl, C_{2-10} alkenyl or C_{1-10} alkenoyl, subject to the proviso that where B, B' or B" is $-L(ML^1)_q$, L^1 is not substituted by the substituents $-C(O)R^a$, $-C(NR^a)R^b$, $-C(O)NR^aR^b$ or $-SO_2R^a$ wherein R^a and R^b are each independently, hydrogen or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O, to a patient with carcinoma of the lungs, pancreas, thyroid, bladder or colon, myeloid leukemia or villous colon adenoma.